REMARKS/ARGUMENTS

Claims 10, 12-21 and 36-43 were examined in the above-identified application. Claims 10, 14, 39 and 43 have been amended. Claim 15 has been canceled without prejudice to Applicants' right to prosecute the subject matter of the claim in a related, co-pending application. Support for these amendments claims is identified in the following remarks. No new matter is added by the amendments.

All prior rejections have been withdrawn and new rejections have been set forth. Applicants believe that the amendments above and the remark below place the claims in condition for allowance and respectfully request the Examiner to reconsider the pending claims.

Rejections under 35 U.S.C. §103(a)

Claims 10-14 and 16-21 and newly added Claims 36-43 stand rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 5,788,963 (1998, IDS) in view of Thurnher *et al.* (1997, IDS) and Ramoner *et al.* (1998, IDS). The Examiner has cited the '963 patent as allegedly teaching "a method for producing an anti-tumor cell, antigen specific cytotoxic T cell (CTL) response comprising administering to a patient an effective amount of human DCs, said DCs having been exposed *in vitro* to the prostate tumor associated antigenic fragment PSM-P1 (SEQ ID NO:1) derived from various sources including tumor cell lysates and purified antigens." The Examiner also cites the '963 patent as allegedly teaching that the DCs are obtained from peripheral blood, have been cryopreserved, have been obtained from a healthy HLA matched donor, are extended life span, and can be administered to a metastatic prostate cancer patient. The Examiner believes that the reference differs from the claimed invention only in that it does not teach the use of BCG in the *in vitro* exposure of the DCs to antigen.

Thurnher *et al.* is cited by the Examiner as allegedly teaching the *in vitro* maturation and activation of DCs with BCG and that the reference further allegedly teaches that

DCs matured in the presence of BCG may also take up tumor antigens and thus, then be capable of activating tumor-reactive T cells in a cytokine milieu that favors the generation of a strong anti-tumor CTL response. The Examiner also believes that the references teaches tumor-antigen loading of DCs cultured in BCG.

Ramoner *et al.* is cited by the Examiner as allegedly further extending the work of Thurnher *et al.* by teaching that BCG 'is a potent activator of human DCs' and allegedly teaching that BCG stimulates the ability of DCs to activate T cells. The Examiner also believes that the reference teaches the BCG could be used in DC based tumor immunotherapy.

The Examiner has combined the references to suggest that "it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to perform a method for producing an anti-tumor cell, antigen specific CTL response comprising administering to a patient an effective amount of human DCs, the DCs having been exposed *in vitro* to the prostate tumor associated antigenic fragment PSM-P1, the DCs having been obtained from peripheral blood, having been cryopreserved, having been obtained from a healthy HLA matched donor, having been extended life span, and having been administered to a metastatic prostate cancer patient, as taught by the '963 patent." It is further believed by the Examiner that "one of ordinary skill in the art would have been motivated to add BCG to the *in vitro* exposure of DCs to antigen for an improved anti-tumor, antigen specific CTL response, given the combined teachings of Thurnher *et al.* and Ramoner *et al.* that 1) BCG causes the maturation of DC and thus, the DCs are capable of activating tumor-reactive T cells in a cytokine milieu that favors the generation of a strong anti-tumor CTL response and 2) BCG 'is a potent activator of human DCs', BCG stimulates the ability of DCs to activate T cells, and BCG could be used in DC based tumor immunotherapy." The Examiner also believes that claims 36 and 40 "comprise only the routine optimization of the claimed method and fall well within the purview of one of ordinary skill in the art at the time of the invention."

Applicants do not agree with the Examiner's summary of the motivation provided by the art or with summary of what the skilled artisan would have considered *prima facie* obvious at the time of the claimed invention. Applicants do not believe that the Examiner has made a proper showing, but in order to further expedite prosecution of certain subject matter

disclosed in the application the claims have been amended. In particular, claim 10 has been amended to recite that the human dendritic cells are "exposed *in vitro* to a soluble, exogenous tissue specific antigen and bacillus Calmette Guerin (BCG) or BCG with lipopolysaccharide (LPS) to induce antigen processing and to promote Major Histocompatibility Complex- (MHC-) class I presentation of the antigen." By this amendment the claim more distinctly recites that the antigen is a soluble, exogenous tissue specific antigen that must be processed within the cell prior to presentation in the context of MHC-class I. Peptides would not be considered an antigen that requires processing by the dendritic cell prior to presentation. Claims 14, 39 and 43 have been amended to delete the recitation of PSMA peptides. Therefore, the '963 patent as summarized by the Examiner is believed to be moot as a obviousness reference to the currently pending claim. As such, the secondary references are not believed to disclose or suggest the current limitations of the pending claims either alone or in any combination with the '963 patent.

It should also be noted that Applicants do not believe that Thurnher *et al* disclose that *in vitro* exposure of DCs to BCG induces a cytokine milieu that favors the generation of a strong anti-tumor CTL response. The passage referred to by the Examiner appears to suggest that the cytokine milieu is induced *in vivo* by the uptake of tumor antigens along with BCG as a consequence of the intra- or peri-tumoral administration of BCG.

Further, Applicants do not believe that claims 36 and 40 merely comprise routine optimization of the claimed method. In particular, the uptake of soluble, exogenous antigen by DCs subsequent to activation and maturation is contrary to the teachings of the art. See page 32, lines 18 through 29 of the specification. The art discloses that exogenous soluble antigen is processed in the MHC class II pathway and cellular antigens, such as bacteria and virus, are processed by the MHC class I pathway for presentation on the surface of DCs. The art further teaches that mature DCs typically do not take up and process antigen, while the present application demonstrates that sufficient soluble antigen is taken up and process by mature DCs to increase the expression of mature DC surface markers including CD8.

Applicants do not believe that claims 10-14, 16-21 and 36-43 as amended and in view of the remarks above are unpatentable over U.S. Patent 5,788,963 in view of Thurnher *et al.* and Ramoner *et al.* and reconsideration of the claims and withdrawal of the rejection is respectfully requested.

Rejections under 35 U.S.C. §112

Claims 36-43 stand rejected under 35 U.S.C. §112, first paragraph, the Examiner believing that the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. In particular, the Examiner does not believe that the specification and the claims as originally filed provide support for the generic invention as recited in claims 36 and 40.

Applicants traverse this ground of rejection. In particular, support for claim 36 can be found throughout the specification. See for example, page 10, lines 11-15, and 19-22, page 18, lines 11-32, and the Examples. Support for claim 40 is explicitly recited in Example 2, but as the example describes a model system, Applicants believe that the use of any soluble exogenous tissue associate antigen will provide a similar result. As generic claims 36 and 40 are believed to be properly described in the specification and claims as filed reconsideration of the rejection of claim 36-43 under 35 U.S.C. §112, first paragraph is respectfully requested.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance and an action to that end is respectfully requested. If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 206-467-9600.

Respectfully submitted,

Dated: 22 August 2005 By: Brian W. Poor

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